

AMENDMENTS TO THE CLAIMS:

Amend the claims as follows:

1. (Currently Amended) A biologically active complex comprising alpha-lactalbumin or a variant of alpha-lactalbumin (α -lactalbumin) at least 70% identical to human alpha-lactalbumin (SEQ ID NO:1) or at least 70% identical to bovine alpha-lactalbumin (SEQ ID NO:2) which is in the apo folding state, or a fragment of either of any of these, and a cofactor which stabilises the complex in a biologically active form, provided that the variant and the fragment comprise a region corresponding to the region of α -lactalbumin which forms the interface between the alpha and beta domains defined by amino acids 34-38 and amino acids 82-86 of SEQ ID NO:1, and wherein the variant and the fragment are at least 100 amino acids in length, and further provided that when the complex comprises full length α -lactalbumin or a variant of α -lactalbumin in which the calcium binding site has been modified so that the affinity for calcium is reduced, or it is no longer functional, the cofactor is other than C18:1:9 cis fatty acid and a cofactor which stabilises the complex in a biologically active form, wherein the alpha-lactalbumin is selected from the group consisting of:
 - (i) an alpha-lactalbumin identified by SEQ ID NO 1 or SEQ ID NO 2,
 - (ii) an alpha-lactalbumin variant which has at least 95 % identity to human alpha-lactalbumin as defined by SEQ ID NO 1 or at least 95 % identity to bovine alpha-lactalbumin as defined by SEQ ID NO 2,
 - (iii) an alpha-lactalbumin fragment comprising amino acid 34-86 of human α -lactalbumin defined by SEQ ID NO 1 and

(iv) an alpha-lactalbumin fragment of an alpha-lactalbumin as identified by SEQ ID NO 1 or SEQ ID NO 2 comprising at least 100 amino acids in length,

wherein the cofactor is an unsaturated fatty acid which has a configuration similar to C18:1:9 or C18:1:11 with the proviso that the cofactor is not C18:1:9 cis (oleic acid).

2. (Currently Amended) A complex according to claim 1 wherein the cofactor has a stereo-specificity similar to [[is a]] cis C18:1:9 and [[or]]cis C18:1:11 fatty acid.

3. (Currently Amended) A complex according to claim 1 wherein the cofactor is cis C18:1:11 fatty acid.

4. (Currently Amended) A complex according to claim 1 which comprises
(ii) an alpha-lactalbumin variant which has at least 95 % identity to human alpha-lactalbumin as defined by SEQ ID NO 1 or at least 95 % identity to bovine alpha-lactalbumin as defined by SEQ ID NO 2,

(iii) an alpha-lactalbumin fragment comprising amino acid 34-86 of human α -lactalbumin defined by SEQ ID NO 1 and

(iv) an alpha-lactalbumin fragment of an alpha-lactalbumin comprising at least 100 amino acids in length

~~a the variant or the fragment, wherein the fragment includes a region corresponding to the region of α -lactalbumin which forms the interface between the alpha and beta domains defined by amino acids 34-38 and amino acids 82-86 of SEQ ID NO:1.~~

5. (Currently Amended) A biologically active complex according to claim 1 which is obtainable by combining

- (i) a cis unsaturated ~~C18:1:9 or C18:1:11~~ fatty acid; and
- (ii)
 - (a) ~~[[α -]]~~an alpha lactalbumin from which calcium ions have been removed, or
 - (b) a variant of alpha-lactalbumin ~~at least 70% identical to human alpha-~~ lactalbumin (SEQ ID NO:1) ~~or at least 70% identical to bovine alpha-lactalbumin (SEQ ID NO:2)~~ from which calcium ions have been removed or which does not have a functional calcium binding site; or
 - (c) a fragment of an alpha-lactalbumin comprising at least 100 amino acids in length from which calcium ions have been removed ~~either of any of these, provided that any fragment comprises a region corresponding to the region of α -lactalbumin which forms the interface between the alpha and beta domains defined by amino acids 34-38 and amino acids 82-86 of SEQ ID NO:1, and wherein the variant and the fragment are at least 100 amino acids in length, and further provided that when (ii) is full length α -lactalbumin or a variant of α -lactalbumin in which the calcium binding site has been modified so that the affinity for calcium is reduced, or it is no longer functional, (i) is other than C18:1:9 cis fatty acid.~~

6. (Currently Amended) A complex according to claim 1 which includes an alpha-lactalbumin variant of ~~α -lactalbumin~~ in which the calcium binding site has been modified so that the affinity for calcium is reduced, or it is no longer functional, ~~and in which the cofactor is C18:1:11 fatty acid.~~

7. (Previously Presented) A complex according to claim 6 wherein the variant has a mutation at a position corresponding to at least one of the K79, D82, D84, D87 or D88 residues of bovine alpha-lactalbumin (SEQ ID NO:2).

8. (Currently Amended) A complex according to claim 7 which includes a D87A variant of $[[\alpha-]]$ alpha lactalbumin (SEQ ID NO:3) or D87N variant of α -lactalbumin (SEQ ID NO:4).

9. (Currently Amended) A complex according to claim 1 which comprises an alpha lactalbumin fragment of ~~α -lactalbumin or a variant thereof~~, and where the fragment includes the entire region from amino acid 34-86 of SEQ ID NO:1 ~~or SEQ ID NO:2~~.

10. (Currently Amended) A complex according to claim 1 wherein the $[[\alpha-]]$ alpha lactalbumin is

(i) human $[[\alpha-]]$ alpha lactalbumin as defined by $[[()]]$ SEQ ID NO:1 $[[()]]$ or

(ii) bovine $[[\alpha-]]$ alpha lactalbumin as defined by $[[()]]$ SEQ ID NO:2 $[[()]]$ or

(iii) an alpha lactalbumin $[[a]]$ variant which has at least $[[70]]$ 95% $[[identical]]$ identity to SEQ IN NO:1 or SEQ ID NO:2~~either of these~~.

11. (Currently Amended) A complex according to claim 10 wherein the $[[\alpha-]]$ alpha lactalbumin is human α -lactalbumin (SEQ ID NO:1).

12. (Currently Amended) A complex according to claim 10 wherein the [[α]]alpha lactalbumin variant is mutant bovine α -lactalbumin which includes an S70R mutation (SEQ ID NO:5).

13. (Previously Presented) A complex according to claim 1 which further comprises calcium ions.

14. (Previously Presented) A pharmaceutical composition comprising a complex according to claim 1 in combination with a pharmaceutically acceptable carrier.

Claim 15. (Canceled)

Claim 16. (Canceled)

Claim 17. (Canceled)

18. (Previously Presented) A complex according to claim 1 wherein the cofactor is an unsaturated cis fatty acid which stabilises the complex in a biologically active form.

19. (Previously Presented) A complex according to claim 1 wherein the cofactor is an C18:1 cis fatty acid which stabilises the complex in a biologically active form.

20. (Currently Amended) A complex according to claim 2, wherein the variant of alpha-lactalbumin comprises conservative amino acid substitutions~~is at least 95 % identical to human alpha-lactalbumin (SEQ ID NO:1) or at least 95 % identical to bovine alpha-lactalbumin (SEQ ID NO:2).~~

21. (Previously Presented) A complex according to claim 20, wherein the variant of alpha-lactalbumin is at least 95 % identical to human alpha-lactalbumin (SEQ ID NO:1).

Claim 22. (Canceled)

23. (Currently Amended) A complex according to claim 3, wherein the variant of alpha-lactalbumin comprises conservative amino acid substitutions~~is at least 95 % identical to human alpha-lactalbumin (SEQ ID NO:1) or at least 95 % identical to bovine alpha-lactalbumin (SEQ ID NO:2).~~

24. (Currently Amended) A complex according to claim 23, wherein the variant of alpha-lactalbumin [[is]]has at least 95 % [[identical]]identity to human alpha-lactalbumin (SEQ ID NO: 1).

25. (Currently Amended) A complex according to claim 24, wherein the variant of alpha-lactalbumin ~~at least 95 % identical to human alpha-lactalbumin (SEQ ID NO: 1)~~ comprises conservative amino acid substitutions.

26. (New) The complex according to claim 1, wherein the cofactor is an C16-18cis unsaturated fatty acid.

27. (New) The complex according to claim 1, wherein the cofactor is an unsaturated fatty acid selected from the group of: C18:1:11cis , C18:1:6cis, C18:2:9,12cis, C16:1:9cis, C18:3:6,9,12cis and C18:3:9,12,15cis.

28. (New) The complex according to claim 1 wherein the cofactor is selected from the group of: C18:1:11cis , C18:1:6cis, C18:3:6,9,12cis and C18:3:9,12,15cis.

29. (New) A biologically active complex comprising alpha-lactalbumin and a cofactor which stabilises the complex in a biologically active form, wherein the cofactor is oleic acid (C18:1:9cis) and wherein the alpha-lactalbumin is selected from the group consisting of:

- (i) bovine alpha-lactalbumin identified by SEQ ID NO 2.
 - (ii) an alpha-lactalbumin variant which has at least 95 % identity to human alpha-lactalbumin as defined by SEQ ID NO 1 or at least 95 % identity to bovine alpha-lactalbumin as defined by SEQ ID NO 2,
 - (iii) an alpha-lactalbumin fragment comprising amino acid 34-86 of human α -lactalbumin defined by SEQ ID NO 1 and
 - (iv) an alpha-lactalbumin fragment of an alpha-lactalbumin as identified by SEQ ID NO 1 or SEQ ID NO 2 comprising at least 100 amino acids in length,
- wherein the alpha-lactalbumin is not to human alpha-lactalbumin as defined by SEQ ID NO 1.

30. (New) The complex according to claim 29 which includes an alpha-lactalbumin variant in which the calcium binding site has been modified so that the affinity for calcium is reduced, or it is no longer functional.

31. (New) The complex according to claim 29 wherein the variant has a mutation at a position corresponding to at least one of the K79, D82, D84, D87 or D88 residues of bovine alpha-lactalbumin as defined by SEQ ID NO 2.

32. (New) The complex according to claim 29, which includes a D87A or D87N variant of alpha-lactalbumin as defined by SEQ ID NO 3 and SEQ ID NO 4, respectively.

33. (New) The complex according to claim 29, wherein the alpha-lactalbumin variant is mutant bovine α -lactalbumin which includes an S70R mutation as defined by SEQ ID NO 5.

34. (New) The complex according to claim 29, wherein the alpha-lactalbumin is

- (i) bovine alpha-lactalbumin as defined by SEQ ID NO 2 or
- (ii) an alpha-lactalbumin variant at least 95 % identical to SEQ ID NO 1 or

SEQ ID NO 2.

35. (New) The complex according to claim 29, which comprises an alpha-lactalbumin fragment and where the fragment includes the entire region from amino acid 34-86 of human alpha-lactalbumin as defined by SEQ ID NO 1.